Chronic suppurative lung disease and bronchiectasis in children and adults in Australia and New Zealand

A position statement from the Thoracic Society of Australia and New Zealand and the Australian Lung Foundation

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ABSTRACT

- Consensus recommendations for managing chronic suppurative lung disease (CSLD) and bronchiectasis, based on systematic reviews, were developed for Australian and New Zealand children and adults during a multidisciplinary workshop.
- The diagnosis of bronchiectasis requires a high-resolution computed tomography scan of the chest. People with symptoms of bronchiectasis, but non-diagnostic scans, have CSLD, which may progress to radiological bronchiectasis.
- CSLD/bronchiectasis is suspected when chronic wet cough persists beyond 8 weeks. Initial assessment requires specialist expertise. Specialist referral is also required for children who have either two or more episodes of chronic (> 4 weeks) wet cough per year that respond to antibiotics, or chest radiographic abnormalities persisting for at least 6 weeks after appropriate therapy.
- Intensive treatment seeks to improve symptom control, reduce frequency of acute pulmonary exacerbations, preserve lung function, and maintain a good quality of life.
- Antibiotic selection for acute infective episodes is based on results of lower airway culture, local antibiotic susceptibility patterns, clinical severity and patient tolerance. Patients whose condition does not respond promptly or adequately to oral antibiotics are hospitalised for more intensive treatments, including intravenous antibiotics.
- Ongoing treatment requires regular and coordinated primary health care and specialist review, including monitoring for complications and comorbidities.
- Chest physiotherapy and regular exercise should be encouraged, nutrition optimised, environmental pollutants (including tobacco smoke) avoided, and vaccines administered according to national immunisation schedules.
- Individualised long-term use of oral or nebulised antibiotics, corticosteroids, bronchodilators and mucoactive agents may provide a benefit, but are not recommended routinely.

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Frequently used abbreviations

c-HRCT	Chest high-resolution computed tomography
COPD	Chronic obstructive pulmonary disease
CSLD	Chronic suppurative lung disease
FEV_1	Forced expiratory volume in 1 second
PsA	*Pseudomonas aeruginosa*
QoL	Quality of life
RCT	Randomised controlled trial

Although regarded in high-income countries as an orphan disease,[1,2] bronchiectasis remains a major contributor to chronic respiratory morbidity in less-affluent populations, both Indigenous[3] and non-Indigenous.[1,4,5] Moreover, delays in diagnosis of bronchiectasis of years to decades commonly occur in children[4] and adults,[6] and it is likely that many remain undiagnosed and untreated, risking premature and accelerated pulmonary decline.[7,8] This position statement from the Thoracic Society of Australia and New Zealand (TSANZ) and the Australian Lung Foundation (ALF), developed at a multidisciplinary workshop, presents consensus recommendations for managing chronic suppurative lung disease (CSLD), including bronchiectasis, in children and adults in settings other than remote and rural Indigenous Australian communities; recommendations for these communities are available elsewhere.[3] This statement provides an overview and is not intended to replace individualised specialist care. As with all guidelines, it does not substitute for sound clinical judgement, particularly when addressing such a phenotypically heterogeneous condition as bronchiectasis.[9] The development process undertaken by the working group is outlined in Box 1 and the full position statement will be available on the TSANZ website (http://www.thoracic.org.au/).

Objectives

1. To increase awareness of CSLD and bronchiectasis in children and adults.
2. To encourage earlier diagnosis and improved management of CSLD and bronchiectasis.
3. To present an Australian and New Zealand consensus on appropriate management of CSLD and bronchiectasis.

Bronchiectasis and CSLD — incidence, diagnosis and mortality rates

The only available Australasian data on CSLD and bronchiectasis are in children aged under 15 years. In New Zealand, the national incidence of bronchiectasis is 3.7/100 000 per year,[4] which is almost twice that of cystic fibrosis, while in Central Australian Indigenous children the estimated prevalence of bronchiectasis is at least 1470/100 000.[12] Estimated bronchiectasis prevalence rates in the United States range from 4.2/100 000 in 18–34-year-olds to 272/100 000 in those over 75 years.[13] Patients with bronchiectasis were found to spend two more days in hospital and have higher annual medical care expenditure (by US$5681) than age- and sex-matched controls with other chronic illnesses, such as diabetes and heart failure.[13]

Bronchiectasis can be misdiagnosed as, or coexist with, other chronic respiratory diseases. Between 29% and 50% of people with chronic obstructive pulmonary disease (COPD) have bronchiectasis,[3] as do as many as 40% of newly referred patients with difficult-to-control asthma and a chronic cough;[14] thus it is likely that many people with chronic respiratory symptoms due to CSLD or bronchiectasis remain undiagnosed.

Bronchiectasis causes premature death.[15] The only published Australian mortality data for bronchiectasis are from a hospital-based cohort of 61 adults (mean [SD] age, 42 [15] years) in Central Australia where 11.5% died within 12 months.[15] In other countries, mortality rates in adults with bronchiectasis vary widely, from 58% survival at 4 years (Turkey) and 75% survival at 8.8 years (Finland) to 81% survival at 14 years (Scotland).[16] Complications and comorbidities associated with bronchiectasis extend beyond the respiratory system and include cardiac and psychological effects.[17]

Definitions and their limitations

The definitions of bronchiectasis, CSLD and protracted bacterial bronchitis are compromised by overlapping symptoms and signs that are not specific to an individual condition (Box 2). Thus, some clinicians, particularly paediatricians, use the term CSLD for all three conditions. Whether these three conditions are different, or are part of a spectrum of disease severity, remains undetermined.[18] While the principles of managing all three conditions are similar, there are few published intervention studies, especially for managing patients with CSLD. Consequently, many of the recommendations for CSLD are extrapolated from studies of bronchiectasis. Until further evidence is available, we believe including CSLD is important given (i) the spectrum of disease; (ii) the increasing evidence that early diagnosis and treatment improves outcomes and reduces pulmonary decline;[8,26,27] and (iii) the difficulties of providing robust definitions.

Recommendation 1

1a. CSLD describes a clinical syndrome of respiratory symptoms and/or signs. Symptoms of chronic endobronchial suppuration are a continuous, wet or productive cough for more than 8 weeks, with or without other features, such as exertional dyspnoea, symptoms of reactive airway disease, recurrent chest infections, growth failure, clubbing, hyperinflation or chest wall deformity. In children, triggers for referral to a specialist include: (i) two or more episodes of chronic (> 4 weeks) wet cough per year responding to antibiotics; and (ii) a chest radiograph abnormality persisting for more than 6 weeks after appropriate therapy.

1b. Bronchiectasis refers to CSLD with the presence of radiological features on a chest high-resolution computed tomography (c-HRCT) scan.

Grade: strong; evidence: not applicable

Aetiology and investigations of a patient with CSLD/bronchiectasis

Radiology

Plain chest radiographs are insensitive, and c-HRCT (conventional or multidetector) scans, despite their limitations (Box 2), remain the diagnostic gold standard. As children, adolescents and young

1 Development process of the position statement

GRADE approach to guideline development

The recommendations were based on the available evidence (Box 5). Principles of evidence-based medicine and the revised GRADE[10] approach to guideline development were used to categorise recommendations into: strong, weak, or no specific recommendation.[10]

The implications of a strong recommendation are:[10]

- For patients — most people in your situation would want the recommended course of action and only a small proportion would not; request discussion if the intervention is not offered.
- For clinicians — most patients should receive the recommended course of action.
- For policymakers — the recommendation can be adopted as a policy in most situations.

The implications of a weak recommendation are:

- For patients — most people in your situation would want the recommended course of action, but many would not.
- For clinicians — you should recognise that different choices will be appropriate for different patients and that you must help each patient to arrive at a management decision consistent with her or his values and preferences.
- For policymakers — policy making will require substantial debate.

The levels of evidence provided by GRADE are:

High = Further research is very unlikely to change our confidence in the estimate of effect.

Moderate = Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low = Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low = Any estimate of effect is very uncertain.

When relative risk was not available in publications, the decision to upgrade the evidence was based primarily on the likelihood of further research having an effect on the recommendation.

Database search

An updated search (from a previous search in October 2007[3]) was conducted in July 2009 by one of us (A B C) using the text words "bronchiectasis" or "suppurative lung disease" and "controlled trials" in the PubMed and Cochrane Central Library databases. Only full articles published in English were retrieved. A draft of this document was circulated to all authors before a workshop held in Brisbane on 7 August 2009.

Consensus process

Recommendations were drafted and finalised by complete agreement by the eight authors who attended the workshop. The assigned evidence level (defined above) of recommendations was also obtained (complete agreement by the workshop attendees). This document and a summary table were then circulated to the entire group of 13 authors for assessment using the GRADE descriptors.[10] Strength of recommendations were assigned by formal voting rules,[11] and agreement with a statement by more than 75% of the group was defined a priori as consensus.

GRADE = Grading of Recommendations Assessment, Development and Evaluation ◆

2 Definitions

Bronchiectasis

Bronchiectasis is a radiological or pathological diagnosis characterised by abnormal irreversible bronchial dilatation. It is mostly diagnosed by a chest high-resolution computed tomography (c-HRCT) scan, which is the current diagnostic gold standard. However, a radiological diagnosis of bronchiectasis may be reported by radiologists in patients with interstitial lung diseases (eg, pulmonary fibrosis) where traction on the airways causes bronchial dilatation. Traction bronchiectasis in the absence of a chronic productive cough will not be considered further in this position statement.

In adults, the dominant presenting symptom is a chronic or recurrent productive cough. In children, the cough is wet rather than productive, as young children do not usually expectorate,[18] and after treatment the cough often temporarily resolves.[19]

Chronic suppurative lung disease (CSLD)

CSLD describes a clinical syndrome in which there are symptoms indicating chronic endobronchial suppuration (see Recommendation 1a, *page 357*) with or without evidence of radiological bronchiectasis on c-HRCT scans. However, absence of symptoms (other than wet cough) and signs does not reliably exclude either bronchiectasis or CSLD. Lung abscess and empyema (previously considered as within the CSLD spectrum) have distinct radiological characteristics and are not discussed here.

Chronic infective bronchitis and protracted bacterial bronchitis

Most patients have a productive or wet cough for several years before a diagnosis is made.[5,12] Pathobiological studies and clinical observations suggest many patients have bronchitis initially that, if left untreated, gradually evolves into bronchiectasis.[18] The entity of protracted bacterial bronchitis has been used in relation to children in whom a prolonged wet cough completely resolves after antibiotic treatment.[18] Many of these children were previously misdiagnosed with asthma and had responded poorly to asthma therapies. In some settings these children would have been classified as having "difficult or severe asthma".[18,20] We also suspect that a proportion of adults diagnosed with "difficult" and/or neutrophilic asthma in fact have bronchiectasis as their primary diagnosis. In a recent study, 40% of newly referred adults with "difficult asthma" were found to have bronchiectasis.[14] While the evidence is limited, it is highly likely that, in some circumstances, untreated bronchitis progresses to bronchiectasis and/or airflow limitation.[18] The definitions of bronchiectasis, CSLD and protracted bacterial bronchitis have limitations, as their associated symptoms and signs overlap and lack specificity. However, absolute reliance on a radiology-based definition is also unsatisfactory for the following reasons:

1. It is not known when diagnostic radiological changes of bronchiectasis appear in the course of the illness in patients with symptoms of CSLD/bronchiectasis. Studies in adults found that bronchography (the old diagnostic gold standard) is superior to a c-HRCT scan at detecting bronchiectasis, especially when mild disease is present.[21] Another study reported that by using a 16-slice computed tomography scan of the chest (contiguous 1-mm slices), 40 extra lobes with evidence of bronchiectasis were identified in 53 adults previously examined by conventional c-HRCT scans.[22]

2. One of the key signs of bronchiectasis on c-HRCT scans, increased bronchoarterial ratio, is significantly influenced by age.[23] However, it remains to be determined whether a lower bronchoarterial ratio should be used in children.

3. At least two c-HRCT scans are required to fulfil the criteria of "irreversible dilatation". Nonetheless, performing more than one c-HRCT scan purely for diagnostic, as opposed to management, reasons is controversial because of the small, but increased, radiation-induced cancer risk[24] and, moreover, is often impractical in some settings.

4. c-HRCT scans performed during various clinical states, such as during an acute respiratory illness, immediately after treatment and when clinically stable, can yield different results.[3,25] ◆

adults are at greater risk from radiation-induced cancers later in life,[24] the c-HRCT protocol must ensure the lowest possible radiation exposure to obtain adequate assessment.[28]

Recommendation 2

Patients with symptoms and/or signs of CSLD require a c-HRCT scan to confirm the diagnosis and to assess severity and extent of bronchiectasis. Specialist advice is preferred before ordering a c-HRCT scan for children.

Grade: strong; evidence: moderate

Aetiological associations

Several causative and associated factors are described for CSLD/bronchiectasis (Box 3). Identifying aetiology and disease severity can influence management, including treatment intensity.[29,30] Investigations for specific causes of CSLD/bronchiectasis are recommended (Box 4), even though many patients will not have an identifiable aetiology.[3,4,9]

Assessment of severity

In addition to routine clinical data (cough, sputum, exacerbation rate, wellbeing, etc) and radiological assessment, objective tests provide information about disease severity and prognosis.

Lung function

Bronchiectasis is primarily an airway disease and, although spirometry data are classically obstructive, a restrictive pattern is also recognised.[5] Spirometry and lung-volume measurements should be performed at diagnosis, and spirometry repeated at each review, even though these tests can be relatively insensitive in mild disease and in children.[12] Many patients have a gradual deterioration in lung function over time.[5,7] If serial pulmonary function tests indicate disease progression, a step-up in therapy is usually required. Studies in children show that spirometric volumes can stabilise and even improve.[8,26,27] In adults with moderate-to-severe bronchiectasis, mortality risk is associated with the degree of lung-function impairment.[16] Other tests, including complex pulmonary-function tests and the 6-minute walk test, are sometimes used for determining functional impairment, but these are not discussed further.

Microbiology

Surveillance of airway or sputum microbiology helps guide antibiotic therapy in CSLD/bronchiectasis,[31] especially if there is deterioration or inadequate response to current treatment. The most common pathogens recovered from children are non-typeable *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Moraxella catarrhalis*.[4,32] In adults, *Pseudomonas aeruginosa* and non-typeable *H. influenzae* predominate.[33] About 25%–45% of airway samples fail to grow pathogenic bacteria. As disease progresses, the microbiological flora changes, often with *P. aeruginosa* appearing in more advanced disease and predicting a worse prognosis.[33] *Aspergillus* and non-tuberculous mycobacteria species are detected in some adults with bronchiectasis, although their pathogenic role is often uncertain.[33] Nonetheless, non-tuberculous mycobacteria have been implicated in exacerbations[31] and pulmonary deterioration.[34]

Other tests

Pulmonary arterial hypertension complicates severe CSLD/bronchiectasis.[12] In advanced disease, chronic or nocturnal hypoxaemia is common, and selected patients require arterial blood gas, an echocardiogram and an overnight oxygen assessment.

Recommendation 3

When CSLD/bronchiectasis is present, obtaining further information about specific underlying causes may determine subsequent investigation and management. History taking should include questions on:

- parameters suggestive of cystic fibrosis (family history, pancreatitis, chronic gastrointestinal symptoms, male infertility); and
- underlying immune deficiency (male infertility, recurrent sinusitis, extrapulmonary infections including discharging ears and severe dermatitis).

Grade: strong; evidence: moderate

Recommendation 4

When CSLD/bronchiectasis is present, perform or refer for baseline investigations (Box 4).

Grade: strong; evidence: moderate

Management (Box 5)

Early and effective management reduces short- and long-term morbidity.[8,26,27,40] In primary ciliary dyskinesia, adults diagnosed late have significantly poorer lung function.[41] With appropriate treatment, lung disease complicating primary immunodeficiency should not deteriorate.[8,27] In a Melbourne cohort, longer duration of chronic productive cough was related to reduced lung function.[9] At the initial referral, the mean percentage predicted, forced expiratory volume in 1 second (FEV_1) in those in the cohort with chronic cough from childhood was 18% lower than those with adult-onset symptoms.[9]

Recommendation 5

Aim to optimise general wellbeing, symptom control, lung function and quality of life (QoL); and to reduce exacerbation frequency and prevent excessive decline in lung function. This may require intensive medical therapy.

Grade: strong; evidence: high

Antibiotics

CSLD/bronchiectasis arises from infection and an ineffective host immune response involving uncontrolled recruitment and activation of inflammatory cells within the lower airways.[42] The subsequent release of mediators, such as proteases and free radicals, causes bronchial-wall injury and dilatation.[42] Consequently, intensive antibiotic treatments are advocated to reduce the microbial load. For acute exacerbations, depending on the severity of the episode, oral antibiotics and ambulatory care are usually tried first.[19] More severe exacerbations require hospitalisation with intravenous antibiotics combined with intensified physiotherapy and other airway clearance methods, including nebulised therapy.[19,40]

Response to therapy includes reduction in sputum volume and purulence, improvement in cough characteristics (wet to dry or cessation of cough), general wellbeing, QoL and markers of systemic inflammation (C-reactive protein), demonstration of microbial clearance, and "return to baseline" state.[19,40]

Prolonged oral or inhaled antibiotic treatments are sometimes used to improve QoL and to prevent exacerbations, although the evidence is limited and the possibility of developing antibiotic resistance is of concern. There is increasing interest in macrolides for this purpose; however, further studies are required to establish their role in CSLD/bronchiectasis. Additionally, before using macrolides long-term, the presence of non-tuberculous mycobacteria

3 Aetiologies and factors associated with bronchiectasis

- Congenital causes (eg, Mounier-Kuhn syndrome, Young's syndrome)
- Chronic obstructive pulmonary disease and smoking
- Cystic fibrosis
- Mucociliary dysfunction (eg, primary ciliary dyskinesia)
- Primary or secondary immune deficiency (eg, hypogammaglobulinaemia, lung and bone-marrow transplantation, malignancy, HIV/AIDS)
- Pulmonary fibrosis and pneumoconiosis (eg, silicosis)
- Post-obstruction (eg, with a foreign body)
- Post-infection (eg, tuberculosis, adenovirus, recurrent pneumonia)
- Recurrent small-volume aspiration (eg, from upper airway secretions or gastric contents)
- Systemic inflammatory diseases (eg, rheumatoid arthritis, sarcoidosis) ◆

4 Minimum investigations for bronchiectasis

The minimum investigations are:

- A full blood count and tests for levels of the major immunoglobulin classes IgG, IgA, IgM, and IgG subclasses
- A sweat test
- Culture of airway secretions, including specialised cultures for mycobacteria, particularly non-tuberculous mycobacteria, in sputum-producing patients
- Spirometry and lung volumes (when aged > 6 years)
- Serological tests for *Aspergillus*, and total IgE level in adults
- Test for primary ciliary dyskinesia in children (if expertise available) — exhaled fractional nasal nitric oxide and/or nasal ciliary brushings

In addition, consider the following:

- Test for cystic fibrosis transmembrane conductance regulator (*CFTR*) gene mutations
- Bronchoscopy for foreign body or airway abnormality, and to obtain specimens for culture of respiratory pathogens, including mycobacteria
- Barium swallow
- Additional immunological tests — total IgE level in children; neutrophil function tests and lymphocyte subsets; and antibody responses to protein and polysaccharide antigens (eg, tetanus toxoid and pneumococcal vaccination)
- Test for primary ciliary dyskinesia (in adults when expertise for this is available) — exhaled fractional nasal nitric oxide and/or nasal ciliary brushings
- Test for HIV
- Echocardiogram, especially in adults (when concerned about pulmonary hypertension) ◆

5 Possible interventions and the evidence base for management of chronic suppurative lung disease and bronchiectasis

	Evidence type/study	Summary of results	Notes
Antibiotics (by type)			
General	Cochrane review, other systematic review*	Generally beneficial. See section on Antibiotics (*page 359*)	Antibiotic resistance
Macrolides	RCTs and review for 2–6 months*	Exacerbations significantly reduced in treatment arm; sputum volume and symptoms reduced; some patients showed improvement in pulmonary function tests*	Concerns over antibiotic resistance
Nebulised tobramycin	Double-blind crossover RCT in 30 patients with PsA, 6 months in each arm*	Fewer admissions and days in hospital in tobramycin arm	Antibiotic resistance; nebulised tobramycin poorly tolerated by some patients*
Antibiotics (by duration)			
Short term (< 1 month)	Several cohort studies*	General clinical improvement	
Medium term (1–11 months)	Cochrane review, other systematic reviews*	Improvement with amoxycillin and macrolides (see above). Adults with PsA had shorter hospitalisations, but no change in QoL*	
Long term (⩾ 12 months)	RCTs*	Adults with PsA had fewer admissions and days in hospital.* Reduced general disability in those taking tetracycline compared with placebo*	
Anti-inflammatories			
Oral NSAIDs	Cochrane review*	No RCTs	Cohort study of indomethacin (25 mg three times a day for 28 days) reduced neutrophil chemotaxis, but no change in sputum albumin, elastase or myeloperoxidase levels*
Inhaled indomethacin	Cochrane review[35]	RCT in 25 adults, some with CSLD. Reduced sputum volume and improved dyspnoea score	
Mucolytics			
Bromhexine	Cochrane review*	Studies only in acute phase	Not universally available
Recombinant human deoxyribonuclease	Systematic review*	Increased exacerbation rate and accelerated decline in FEV_1	
Airway clearance			
Chest physiotherapy	Cochrane review* and RCTs[36,37]	Two small trials in patients with bronchiectasis. Recent RCT[37] showed benefit for cough and subjective scores, exercise capacity and 24-hour sputum volume. A study in children showed improvement in sputum volume and FEV_1[36]	
Inhaled hyperosmolar agents	Cochrane review, additional RCT (non-blinded) using 7% hypertonic saline*	Two small short-term studies of mannitol showed benefit in QoL only	
Asthma therapies			
Inhaled corticosteroids	Cochrane review[38]	No difference in any outcome when only RCTs of inhaled corticosteroids v placebo were included. Reduced exacerbation rate in adults with PsA	Limited applicability in children, as high doses are used and children are less likely to have PsA
Oral corticosteroids	Cochrane review*	No RCTs	No data*
Anticholinergics	Cochrane review*	No RCTs	No data*
β_2 Agonist	Cochrane review*	No RCTs	No data*
Leukotriene receptor antagonist	Cochrane review*	No RCTs	No data*

CSLD = chronic suppurative lung disease. FEV_1 = forced expiratory volume in 1 second. NSAIDs = non-steroidal anti-inflammatory drugs. PsA = *Pseudomonas aeruginosa*. QoL = quality of life. RCT = randomised controlled trial.

* No other data found by single-reviewer PubMed search — July 2009 (for references, see Chang AB, Grimwood K, Macguire G, et al[3]; and Chang AB, Redding GJ, Everard ML[18]). ◆

5 Possible interventions and the evidence base for management of chronic suppurative lung disease and bronchiectasis (continued from previous page)

	Evidence type/study	Summary of results	Notes
Physical training			
	Cochrane review and RCT, which was included in Cochrane review as an abstract (data changed)*	Pulmonary rehabilitation improves exercise tolerance, no additional advantage of simultaneous inspiratory muscle training	
Oxygen (domiciliary)			
	No data as sole therapy*	Consider data from patients with COPD showing benefit in survival*	
Surgery			
	Cochrane review*	No RCTs. Cohort studies suggest a benefit in selected cases*	Reduction in exacerbation rate similar in medically treated group.* Adverse events of surgery*
Vaccines			
Pneumococcal conjugate and polysaccharide vaccines	Cochrane review[39]	Single RCT in adults that was inclusive of COPD and other chronic lung disease	Advocated, as vaccines reduce pneumococcal infection risk and respiratory infections
Influenza vaccines	Cochrane review*	No RCTs	Advocated in accordance with national guidelines
Acupuncture			
	RCT*	Improvement in QoL but no effect on sputum volume or the 6-min walk test	
Model of follow-up			
Nurse led	Cochrane review*	No difference in exacerbations, but increase in hospitalisations in nurse-led care compared with doctor-led care	Increased health care cost implications

COPD = chronic obstructive pulmonary disease. QoL = quality of life. RCT = randomised controlled trial.
* No other data found by single reviewer search on PubMed (July 2009) (for references, see Chang AB, Grimwood K, Macguire G, et al[3]; and Chang AB, Redding GJ, Everard ML[18]). ◆

should be excluded in adults and in older children capable of providing sputum samples.[43]

Recommendation 6

Antibiotic selection (Box 6) is based on lower airway culture results (sputum or bronchoscopy washings) when available, local antibiotic susceptibility patterns, clinical severity and patient tolerance, including allergy.

Grade: strong; evidence: moderate

Recommendation 7

In patients not requiring hospitalisation for an acute exacerbation of CSLD/bronchiectasis, oral antibiotics are prescribed for at least 10 days. Close follow-up to assess treatment effect is necessary.

Grade: strong; evidence: low

Recommendation 8

An inadequate response to antibiotic treatment should prompt repeat of lower airway cultures and assessment of whether hospital admission is needed.

Grade: strong; evidence: moderate

Recommendation 9

Patients with an acute exacerbation of CSLD/bronchiectasis which does not respond to oral antibiotic therapy should receive supervised hospital-based therapy, including intensive airway clearance strategies, and intravenous antibiotics determined by the latest lower-airway culture results. In most cases, this requires hospitalisation for at least 7 days.

Grade: strong; evidence: moderate

Recommendation 10

Long-term oral antibiotics, including macrolides, should not be prescribed routinely. They may, however, be considered for a trial in selected patients (eg, those with frequent respiratory exacerbations [more than six exacerbations and/or more than two hospitalisations over 12 months] or more than 6 months of continuous symptoms; the frequency and time frames are arbitrary and based on expert opinion). Before commencing macrolides, non-tuberculous mycobacterial infection should be excluded in all patients capable of providing a sputum specimen.

Grade: strong; evidence: moderate

6 Empirical antibiotic therapy and treatment for specific pathogens — chronic suppurative lung disease and bronchiectasis

	Mild-to-moderate exacerbation (oral therapy)	Severe exacerbation (intravenous therapy)
Initial empirical therapy*	Amoxycillin–clavulanate or doxycycline†	*Children:* cefuroxime,‡ cefotaxime or ceftriaxone. *Adults:* ticarcillin–clavulanate or ceftazidime ± tobramycin§
Haemophilus influenzae		
β-Lactamase negative	Amoxycillin	Ampicillin
β-Lactamase positive	Amoxycillin–clavulanate or doxycycline†	Cefuroxime,‡ cefotaxime or ceftriaxone
Streptococcus pneumoniae	Amoxycillin	Benzylpenicillin G
Moraxella catarrhalis	Amoxycillin–clavulanate	Cefuroxime,‡ cefotaxime or ceftriaxone
Staphylococcus aureus	Dicloxacillin/flucloxacillin	Flucloxacillin
Methicillin-resistant *Staphylococcus aureus*	Seek specialist advice	Seek specialist advice
Pseudomonas aeruginosa	Ciprofloxacin (maximum of 14 days)	Children and adults: ticarcillin–clavulanate or ceftazidime ± tobramycin§
Non-tuberculous mycobacteria	Seek specialist advice	Seek specialist advice

* In addition to clinical severity, initial empirical therapy is also guided by any previous lower-airway culture results (sputum or bronchoscopy washings), local antibiotic susceptibility patterns and prior responses to antibiotic treatments. In children too young to expectorate sputum and when no previous lower-airway culture results are available, prescribed empirical antibiotic therapy should be active against *H. influenzae*, *S. pneumoniae* and *M. catarrhalis*, the respiratory bacterial pathogens most commonly found in this age group. † Doxycycline is used only in adults and children over 8 years of age. ‡ Available in New Zealand. § Emerging evidence in adults (but not children) indicates that treating *P. aeruginosa* infection with combined β-lactam and aminoglycoside antibiotic therapy provides no additional clinical benefit and is associated with more frequent adverse events than treatment with a single β-lactam agent. ◆

Recommendation 11

Nebulised antibiotics, such as gentamicin, tobramycin and colistin, should not be prescribed routinely. However, a therapeutic trial in selected patients with frequent exacerbations (as per Recommendation 10) may be considered.

Grade: strong; evidence: moderate

Bronchodilators and corticosteroids

Patients with CSLD/bronchiectasis may have coexistent asthma with wheeze and/or dyspnoea that is responsive to β_2-agonist medications. Reports on asthma symptoms in those with CSLD/bronchiectasis vary from 11% to 46%.[2,44] While, in some studies, bronchiectasis is ascribed to asthma, it is more likely in such cases that asthma was initially misdiagnosed or coexisted with CSLD/bronchiectasis.[18,20] When present, asthma therapies should be used in accordance with asthma guidelines.

Inhaled corticosteroids provide, at best, a modest benefit in CSLD/bronchiectasis, including in patients with *P. aeruginosa* infection.[38] A Cochrane review found no significant differences between patients receiving very high inhaled corticosteroid doses (2 g/day) and placebo controls.[38]

Recommendation 12

Inhaled and oral corticosteroids should not be routinely prescribed unless there is an established diagnosis of coexisting asthma.

Grade: strong; evidence: low for oral corticosteroids, moderate for inhaled corticosteroids

Recommendation 13

Inhaled bronchodilators should not be routinely prescribed and should be used only on an individual basis.

Grade: strong; evidence: low

Mucolytics and mucoactive agents

Mucoactive agents include mannitol and hypertonic saline. Randomised controlled trials (RCTs) of these agents are in progress with promising efficacy. While there is currently insufficient evidence to justify their use, our recommendation to avoid these mucolytics may change. In contrast, recombinant human deoxyribonuclease (rhDNase), a widely used mucolytic in cystic fibrosis, is harmful in adults with CSLD/bronchiectasis, as it is associated with increased exacerbations and hospitalisations, and more rapid decline in FEV_1.[45]

Recommendation 14

Recombinant human deoxyribonuclease is contraindicated in CSLD/bronchiectasis.

Grade: strong; evidence: high

Recommendation 15

Mucoactive agents, including hypertonic saline and mannitol, are currently not recommended.

Grade: weak; evidence: low

Chest physiotherapy, airway clearance methods, exercise and pulmonary rehabilitation

Despite lacking a robust evidence base, chest physiotherapy to improve airway secretion clearance is standard treatment in children[36] and adults[37,46] with CSLD/bronchiectasis. Nevertheless, available studies suggest chest physiotherapy is beneficial, with improved QoL and exercise capacity and reduced cough and sputum volumes.[37,46] Given the various techniques in airway clearance and the increased efficacy when therapy is individualised,[36] specific chest physiotherapy expertise should be sought.

Pulmonary rehabilitation is employed in several different chronic respiratory conditions. It involves a multidisciplinary approach, including exercise training, self-management education,

and psychosocial and nutritional intervention.[47] Inspiratory muscle training may be beneficial in adults with bronchiectasis. A recent small RCT showed that an 8-week program of pulmonary rehabilitation and inspiratory muscle training significantly improved the incremental shuttle walking test.[48] Unless specific contraindications exist, physical activity should be encouraged.

Recommendation 16

Airway clearance manoeuvres are recommended and a chest physiotherapist's advice should be sought. Chest physiotherapy should be individualised.

Grade: strong; evidence: moderate

Recommendation 17

Adults with CSLD/bronchiectasis and moderately severe, limited exercise tolerance and/or evidence of physical deconditioning should receive pulmonary rehabilitation.

Grade: strong; evidence: moderate

Recommendation 18

Regular physical activity is recommended for children and adults with CSLD/bronchiectasis.

Grade: strong; evidence: high

Nutrition

Poor nutrition (both macro- and micronutrition) compromises innate and adaptive immunity. Studies in other chronic respiratory diseases[49] indicate that poor nutrition may be a risk factor for respiratory exacerbations in CSLD/bronchiectasis.

Recommendation 19

Assess and optimise nutritional status.

Grade: strong; evidence: moderate

Minimisation of further lung injury

Environmental pollutants, including tobacco smoke, exacerbate chronic respiratory disorders and constitute an additional risk factor for those with CSLD/bronchiectasis.

Recommendation 20

Promote elimination of smoking, including second-hand smoke exposure.

Grade: strong; evidence: high

Assessment for comorbidities

Patients with CSLD/bronchiectasis have increased rates of comorbiditiy, including chronic sinusitis, gastro-oesophageal reflux and "asthma-like" disease. It is unknown whether such comorbidities increase the frequency and/or severity of exacerbations or worsen lung injury.

Recommendation 21

Regularly monitor and manage complications and comorbidities (Box 7). When present, these are managed according to standard guidelines.

Grade: strong; evidence: moderate

7 Reviewing patients with chronic suppurative lung disease or bronchiectasis

Review should be undertaken at least annually in adults and 6-monthly in children. Involvement of a multidisciplinary team is preferable, especially at the initial evaluation. The review includes assessment of:

- severity, which includes oximetry and spirometry
- sputum culture
- management of possible complications and comorbidities, particularly for gastro-oesophageal reflux disease, reactive airway disease/asthma, chronic obstructive pulmonary disease, otorhinolaryngeal disorders and dental disease
- Less commonly, patients require assessment for sleep disordered breathing, cardiac complications, and referral for lung transplantation ◆

Other treatments

Various other treatments are available, but with little supportive data (Box 5). Current management strategies have reduced the need for surgical interventions, which carry a small but significant risk of morbidity and mortality. Lung transplantation should be considered in those with end-stage lung disease.

Recommendation 22

Surgery is not normally indicated. There may be some circumstances that require assessment by a multidisciplinary team expert in CSLD/bronchiectasis care.

Grade: strong; evidence: moderate

Public health issues, prevention and appropriate health care delivery

The socioeconomic determinants of health, including their impact on prevalence and disease progression of CSLD/bronchiectasis, cannot be adequately addressed here. Immunisations that prevent acute respiratory infections are recommended despite the lack of specific evidence in relation to bronchiectasis. For pneumococcal immunisation, limited evidence supports using the 23-valent pneumococcal polysaccharide vaccine for reducing acute infective exacerbations.[39]

Delivery of chronic disease programs requires comprehensive and highly skilled primary health care services. Education of primary health care providers should focus on identifying children and adults for appropriate referral and high-quality local management. Initial assessment requires specialist expertise. Like other chronic illnesses, individualised and multidisciplinary case management operating within an interprofessional framework is optimal.[50] Similarly, clinical deterioration should prompt early referral for specialist care. Those with moderate or severe disease are best managed by a multidisciplinary approach to chronic care.

Recommendation 23

All children should have routine vaccinations according to national immunisation schedules. Ensure timely annual influenza vaccination and that pneumococcal vaccines are administered according to national guidelines.

Grade: strong; evidence: moderate

Recommendation 24

Coordination of care among health care providers is necessary. If bronchiectasis is suspected, specialist evaluation is recommended to confirm diagnosis, investigate aetiology, assess baseline severity and develop management plans. Those with moderate or severe disease are best managed by a multidisciplinary approach to chronic care, with individualised case management. Clinical deterioration should prompt early referral to services with CSLD/bronchiectasis expertise.

Grade: strong; evidence: high

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Competing interests

Anne Chang is a Chief Investigator on an NHMRC grant for evaluating azithromycin for bronchiectasis in Indigenous children. Scott Bell has received funding from Boehringer Ingelheim for planning a phase III study of tiotropium in patients with cystic fibrosis. He is a Chief Investigator on an NHMRC grant application evaluating azithromycin and hypertonic saline for adults with bronchiectasis. Cass Byrnes is a Principal Investigator on a New Zealand Health Research Council grant for evaluating azithromycin for bronchiectasis in Indigenous children. She is also the Chief Investigator on a grant for a randomised controlled intervention study of children at high risk of chronic lung disease, and is on the organising committee of the annual respiratory conference sponsored by Boehringer Ingelheim. Keith Grimwood is on the advisory board in NZ for PhiD-CV (synflorix), a pneumoccocal conjugate vaccine. Keith Grimwood and Paul Torzillo are Chief Investigators on an NHMRC grant for evaluating azithromycin for bronchiectasis in Indigenous children.

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